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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,386	10/07/2003	Richard Kolodner	700157-47483-DIV	5982

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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
06/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	**Application No.** 10/680,386	**Applicant(s)** KOLODNER ET AL.	
	Examiner Jeffrey Fredman	**Art Unit** 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 3, 2007 has been entered.

Claim Objections

2. Claim 46 is objected to because of the following informalities:

The word "if" is used after "specimen", but it appears that the word "is" is intended.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 – Written Description

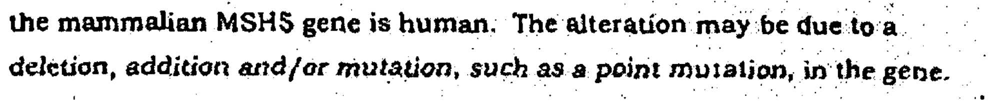
3. The rejection of claims 33 and 35 under 35 U.S.C. 112, first paragraph, is moot in view of the cancellation of these claims.

Claim Rejections - 35 USC § 112 – Scope of Enablement

4. The rejection of claims 13, 14, 17-26, 28-33, 35, 39 and 40 under 35 U.S.C. 112, first paragraph, is moot in view of the cancellation of these claims.

Claim Interpretation

5. The claims have a preamble in which an "alteration" in Msh5 is identified by analysis of a biological sample. The specification at page 5, lines 18-19 notes that an alteration can be due to a deletion or an addition (see below).



the mammalian MSH5 gene is human. The alteration may be due to a *deletion, addition and/or mutation, such as a point mutation,* in the gene.

Thus, any determination of a deletion or addition of MSH5 constitutes an alteration within the meaning of the specification.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 41, 42, 44, 45 and 48 are rejected under 35 U.S.C. 102(a) as being anticipated by Bentz et al (Blood (August 1996) 88(4):1437-1444).

Bentz teaches a method of determining an alteration (see page 1438, column 1, where Bentz teaches the method of comparative genomic hybridization),

Comprising: analyzing a biological sample for an alteration in SEQ ID NO: 1 (see figure 2, where patient 8 had a gain in chromosomal positions which include 6p21.3, the location of the Msh5 gene. This gain inherently represents an alteration in SEQ ID NO:

1 in a human sample, since at the very least, an extra copy of the gene is present in this patient).

With regard to claim 42, Bentz teaches analysis of tissue samples (see page 1438, column 1, first paragraph).

With regard to claim 44, Bentz teaches analysis using DNA in the sample (see page 1438, column 1, subheading "comparative genomic hybridization").

With regard to claim 45, Bentz teaches that the samples are derived from lymphoma tissue (see page 1438, column 1, first paragraph).

With regard to claim 48, Bentz teaches the use of nick translated digoxigenin labeled DNA, which will inherently comprise two oligonucleotides which will hybridize to SEQ ID NO: 1 (see page 1438, column 1).

8. Claims 41, 42, 44, 45 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Yeatman et al (Clin. Exp. Metastatis (May 1996) 14:246-252).

Yeatman teaches a method of determining an alteration (see page 247, column 2, where Yeatman teaches the method of comparative genomic hybridization),

Comprising: analyzing a biological sample for an alteration in SEQ ID NO: 1 (see page 249, figure 2, and table 2 on page 250, which expressly notes that region 6p21.3, the location of Msh5, is deleted in all three colon cancer cell lines). This deletion inherently represents an alteration in SEQ ID NO: 1 in a human sample, since the gene is entirely removed from the sample).

With regard to claim 42, Yeatman teaches analysis of eukaryotic cell samples (see page 247, column 2).

With regard to claim 44, Yeatman teaches analysis using DNA in the sample (see page 247, column 2, subheading "comparative genomic hybridization").

With regard to claim 45, Yeatman teaches that the samples are derived from colon cancer tissue (see table 1).

With regard to claim 48, Yeatman teaches the use of nick translated DNA, which will inherently comprise two oligonucleotides which will hybridize to SEQ ID NO: 1 (see page 247, column 2).

9. Claims 41-43, 47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Sargent et al (EMBO Journal (1989) 8(8):2305-2312).

Sargent teaches a method of determining an alteration (see page 2309, figure 1, northern blot of G7 and page 2310, table 1),

Comprising: analyzing a biological sample for an alteration in SEQ ID NO: 1 (see page 2309, figure 1 and page 2310, where expression of G7 was analyzed in multiple cell lines. The "G7" gene is inherently found to be the MSH5 gene claimed as shown in the alignment below. With regard to points of similiarity, the "G7" gene is located on chromosome 6p21.3 as is the MSH5 gene, and the following is a partial sequence comparison of MSH5 and "G7", where MSH5 is the Qy sequence and "G7" is the database sequence.

```
          Query Match             89.5%;  Score 2596;  DB 68;  Length 3998;
          Best Local Similarity   97.1%;  Pred. No. 0;
          Matches 2675;  Conservative    0;  Mismatches   30;  Indels   51;
Gaps      1;

        Qy    184 tcgccccacagggccttcagacccccttctttccaaaggagcctccaagctcatggcctcc
243
                  |||  |  | |||| |||   | |||           |||||||||||||||||||||||
        Db      6 TCGGTCAGCGGGGCGTTCTCCCACCTGTAGCGACTCAGAGCCTCCAAGCTCATGGCCTCC
65
```

```
      Qy      244 ttaggagcgaacccaaggaggacaccgcagggaccgagacctggggcggcctcctccggt
303
                  |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db       66 TTAGGAGCGAACCCAAGGAGGACACCGCAGGGACCGAGACCTGGGGCGGCCTCCTCCGGC
125

      Qy      304 ttccccagcccggccccagtgccgggccccagggaggccgaggaggaggaagtcgaggag
363
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db      126 TTCCCCAGCCCGGCCCCAGTGCCGGGCCCCAGGGAGGCCGAGGAGGAGGAAGTCGAGGAG
185

      Qy      364 gaggaggagctggccgagatccatctgtgtgtgctgtggaattcaggatacttgggcatt
423
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db      186 GAGGAGGAGCTGGCCGAGATCCATCTGTGTGTGCTGTGGAATTCAGGATACTTGGGCATT
245

      Qy      424 gcctactatgatactagtgactccactatccacttcatgccagatgccccagaccacgag
483
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db      246 GCCTACTATGATACTAGTGACTCCACTATCCACTTCATGCCAGATGCCCCAGACCACGAG
305

      Qy      484 agcctcaagcttctccagagagttctggatgagatcaatccccagtctgttgttacgagt
543
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db      306 AGCCTCAAGCTTCTCCAGAGAGTTCTGGATGAGATCAATCCCCAGTCTGTTGTTACGAGT
365

      Qy      544 gccaaacaggatgagaatatgactcgatttctgggaaagcttgcctcccaggagcacaga
603
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db      366 GCCAAACAGGATGAGAATATGACTCGATTTCTGGGAAAGCTTGCCTCCCAGGAGCACAGA
425

      Qy      604 gagcctaaaagacctgaaatcatattttgccaagtgtggattttggtctggagataagc
663
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db      426 GAGCCTAAAAGACCTGAAATCATATTTTGCCAAGTGTGGATTTTGGTCTGGAGATAAGC
485

      Qy      664 aaacaacgcctcctttctggaaactactccttcatcccagacgccatgactgccactgag
723
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db      486 AAACAACGCCTCCTTTCTGGAAACTACTCCTTCATCCCAGACGCCATGACTGCCACTGAG
545

      Qy      724 aaaatcctcttcctctcttccattattccctttgactgcctcctcaca
771
                  ||||||||||||||||||||||||||||||||||||||||||||||||
      Db      546 AAAATCCTCTTCCTCTCTTCCATTATTCCCTTTGACTGCCTCCTCACACCCCCAGGAGAT
605
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```
      Qy     772                                        gttcgagcacttggagggctg
792
                                                        |||||||||||||||||||||
      Db     606 TTAAGATTTACCCCGATTCCACTGCTGATCCCCTCCCAGGTTCGAGCACTTGGAGGGCTG
665

      Qy     793 ctgaagttcctgggtcgaagaagaatcggggttgaactggaagactataatgtcagcgtc
852
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db     666 CTGAAGTTCCTGGGTCGAAGAAGAATCGGGGTTGAACTGGAAGACTATAATGTCAGCGTC
725

      Qy     853 cccatcctgggctttaagaaatttatgttgactcatctggtgaacatagatcaagacact
912
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db     726 CCCATCCTGGGCTTTAAGAAATTTATGTTGACTCATCTGGTGAACATAGATCAAGACACT
785

      Qy     913 tacagtgttctacagattttaagagtgagtctcacccctcagtgtacaaagtggccagt
972
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db     786 TACAGTGTTCTACAGATTTTTAAGAGTGAGTCTCACCCCTCAGTGTACAAAGTGGCCAGT
845

      Qy     973 ggactgaaggaggggctcagcctctttggaatcctcaacagatgccactgtaagtgggga
1032
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db     846 GGACTGAAGGAGGGGCTCAGCCTCTTTGGAATCCTCAACAGATGCCACTGTAAGTGGGGA
905

      Qy    1033 gagaagctgctcaggctatggttcacacgtccgactcatgacctgggggagctcagttct
1092
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db     906 GAGAAGCTGCTCAGGCTATGGTTCACACGTCCGACTCATGACCTGGGGGAGCTCAGTTCT
965

      Qy    1093 cgtctggacgtcattcagtttttctgctgccccagaatctggacatggctcagatgctg
1152
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db     966 CGTCTGGACGTCATTCAGTTTTTCTGCTGCCCCAGAATCTGGACATGGCTCAGATGCTG
1025

      Qy    1153 catcggctcctgggtcacatcaagaacgtgcctttgattctgaaacgcatgaagttgtcc
1212
                 ||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
      Db    1026 CATCGGCTCCTGGGTCACATCAAGAACGTGCCTCTGATTCTGAAACGCATGAAGTTGTCC
1085

      Qy    1213 cacaccaaggtcagcgactggcaggttctctacaagactgtgtacagtgccctgggcctg
1272
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1086 CACACCAAGGTCAGCGACTGGCAGGTTCTCTACAAGACTGTGTACAGTGCCCTGGGCCTG
1145
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      Qy    1273 agggatgcctgccgctccctgccgcagtccatccagctctttcgggacattgcccaagag
1332
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1146 AGGGATGCCTGCCGCTCCCTGCCGCAGTCCATCCAGCTCTTTCGGGACATTGCCCAAGAG
1205

      Qy    1333 ttctctgatgacctgcaccatatcgccagcctcattgggaaagtagtggactttgagggc
1392
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1206 TTCTCTGATGACCTGCACCATATCGCCAGCCTCATTGGGAAAGTAGTGGACTTTGAGGGC
1265

      Qy    1393 agccttgctgaaaatcgcttcacagtcctccccaacatagatcctgaaattgatgagaaa
1452
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1266 AGCCTTGCTGAAAATCGCTTCACAGTCCTCCCCAACATAGATCCTGAAATTGATGAGAAA
1325

      Qy    1453 aagcgaagactgatgggacttcccagtttccttactgaggttgcccgcaaggagctggag
1512
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1326 AAGCGAAGACTGATGGGACTTCCCAGTTTCCTTACTGAGGTTGCCCGCAAGGAGCTGGAG
1385

      Qy    1513 aatctggactcccgtattccttcatgcagtgtcatctacatccctctgattggcttcctt
1572
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1386 AATCTGGACTCCCGTATTCCTTCATGCAGTGTCATCTACATCCCTCTGATTGGCTTCCTT
1445

      Qy    1573 ctttctattccccgcctgccttccatggtagaggccagtgactttgagattaatggactg
1632
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1446 CTTTCTATTCCCCGCCTGCCTTCCATGGTAGAGGCCAGTGACTTTGAGATTAATGGACTG
1505

      Qy    1633 gacttcatgtttctctcagaggagaagctgcactatcgtagtgcccgaaccaaggagctg
1692
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1506 GACTTCATGTTTCTCTCAGAGGAGAAGCTGCACTATCGTAGTGCCCGAACCAAGGAGCTG
1565

      Qy    1693 gatgcattgctggggggacctgcactgcgagatccgggaccaggagacgctgctgatgtac
1752
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1566 GATGCATTGCTGGGGGACCTGCACTGCGAGATCCGGGACCAGGAGACGCTGCTGATGTAC
1625

      Qy    1753 cagctacagtgccaggtgctggcacgagcagctgtcttaacccgagtattggaccttgcc
1812
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
      Db    1626 CAGCTACAGTGCCAGGTGCTGGCACGAGCAGCTGTCTTAACCCGAGTATTGGACCTTGCC
1685
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          Qy     1813 tcccgcctggacgtcctgctggctcttgccagtgctgcccgggactatggctactcaagg
1872
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     1686 TCCCGCCTGGACGTCCTGCTGGCTCTTGCCAGTGCTGCCCGGGACTATGGCTACTCAAGG
1745

          Qy     1873 ccgcgttactccccacaagtccttggggtacgaatccagaatggcagacatcctctgatg
1932
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     1746 CCGCGTTACTCCCCACAAGTCCTTGGGGTACGAATCCAGAATGGCAGACATCCTCTGATG
1805

          Qy     1933 gaactctgtgcccgaacctttgtgcccaactccacagaatgtggtggggacaaagggagg
1992
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     1806 GAACTCTGTGCCCGAACCTTTGTGCCCAACTCCACAGAATGTGGTGGGGACAAAGGGAGG
1865

          Qy     1993 gtcaaagtcatcactggacccaactcatcagggaagagcatatacctcaaacaggtaggc
2052
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     1866 GTCAAAGTCATCACTGGACCCAACTCATCAGGGAAGAGCATATACCTCAAACAGGTAGGC
1925

          Qy     2053 ttgatcacattcatggccctggtaggcagctttgtgccagcagaggaggccgaaattggg
2112
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     1926 TTGATCACATTCATGGCCCTGGTAGGCAGCTTTGTGCCAGCAGAGGAGGCCGAAATTGGG
1985

          Qy     2113 gcagtagacgccatcttcacacgaattcatagctgcgaatccatctcccttggcctctcc
2172
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     1986 GCAGTAGACGCCATCTTCACACGAATTCATAGCTGCGAATCCATCTCCCTTGGCCTCTCC
2045

          Qy     2173 accttcatgatcgacctcaaccaggtggcgaaagcagtgaacaatgccactgcacagtcg
2232
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     2046 ACCTTCATGATCGACCTCAACCAGGTGGCGAAAGCAGTGAACAATGCCACTGCACAGTCG
2105

          Qy     2233 ctggtccttattgatgaatttggaaagggaaccaacacggtggatgggctcgcgcttctg
2292
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
          Db     2106 CTGGTCCTTATTGATGAATTTGGAAAGGGAACCAACACGGTGGATGGGCTCGCGCTTCTG
2165

          Qy     2293 gccgctgtgctccgacactggctggcacgtggacccacatgcccccacatctttgtggcc
2352
                      |||||||||||||||||||||||||||||||||||||||||||||    |||||||||||
          Db     2166 GCCGCTGTGCTCCGACACTGGCTGGCACGTGGACCCACATGCCCCACAGTCTTTGTGGCC
2225
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        Qy    2353 accaactttctgagccttgttcagctacaactgctgccacaagggcccctggtgcagtat
2412
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        Db    2226 ACCAACTTTCTGAGCCTTGTTCAGCTACAACTGCTGCCACAAGGGCCCCTGGTGCAGTAT
2285

        Qy    2413 ttgaccatggagacctgtgaggatggcaacgatcttgtcttcttctatcaggtttgcgaa
2472
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        Db    2286 TTGACCATGGAGACCTGTGAGGATGGCAACGATCTTGTCTTCTTCTATCAGGTTTGCGAA
2345

        Qy    2473 ggtgttgcgaaggccagccatgcctcccacacagctgcccaggctgggcttcctgacaag
2532
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        Db    2346 GGTGTTGCGAAGGCCAGCCATGCCTCCCACACAGCTGCCCAGGCTGGGCTTCCTGACAAG
2405

        Qy    2533 cttgtggctcgtggcaaggaggtctcagatttgatccgcagtggaaaacccatcaagcct
2592
                   ||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||||
        Db    2406 CTTGTGGCTCGTGGCAAGGAGGTCTCAGACTTGATCCGCAGTGGAAAACCCATCAAGCCT
2465

        Qy    2593 gtcaaggatttgctaaagaagaaccaaatggaaaattgccagacattagtggataagttt
2652
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        Db    2466 GTCAAGGATTTGCTAAAGAAGAACCAAATGGAAAATTGCCAGACATTAGTGGATAAGTTT
2525

        Qy    2653 atgaaactggatttggaagatcctaacctggacttgaacgttttcatgagccaggaagtg
2712
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        Db    2526 ATGAAACTGGATTTGGAAGATCCTAACCTGGACTTGAACGTTTTCATGAGCCAGGAAGTG
2585

        Qy    2713 ctgcctgctgccaccagcatcctctgagagtccttccagtgtcctccccagcctcctgag
2772
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        Db    2586 CTGCCTGCTGCCACCAGCATCCTCTGAGAGTCCTTCCAGTGTCCTCCCCAGCCTCCTGAG
2645

        Qy    2773 actccggtgggctgccatgccctctttgtttccttatctccctcagacgcagagtttta
2832
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        Db    2646 ACTCCGGTGGGCTGCCATGCCCTCTTTGTTTCCTTATCTCCCTCAGACGCAGAGTTTTTA
2705

        Qy    2833 gtttctctagaaattttgtttcatattaggaataaagtttattttgaagaaaaaaa 2888
                   |||||||||||||||||||||||||||||||||||||||||||||||||||| | |
        Db    2706 GTTTCTCTAGAAATTTTGTTTCATATTAGGAATAAAGTTTATTTTGAAGAAAGATA 2761
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Sargent shows that there is an alteration in the expression of G7, which is MSH5, from one cell line relative to another cell line (see page 2310, table 1).

With regard to claim 42, Sargent teaches analysis of eukaryotic cell samples (see page 2309, figure 1, legend).

With regard to claim 43, Sargent teaches analysis using mRNA in the sample (see page 2309, figure 1 and page 2310, table 1, where mRNA is analyzed).

With regard to claim 47, Sargent teaches measurement of the level of expression of G7 in multiple samples (see figure 1 and page 2310, table 1).

With regard to claim 49, Sargent teaches comparison of G7 levels between different cell types, which indicates a functional alteration since the gene is present in some cell types but absent in other cell types (see page 2310, table 1).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bentz et al (Blood (August 1996) 88(4):1437-1444) in view of Therman et al (Human Genetics (1981) 59:93-100).

Bentz teaches a method of determining an alteration (see page 1438, column 1, where Bentz teaches the method of comparative genomic hybridization),

Comprising: analyzing a biological sample for an alteration in SEQ ID NO: 1 (see figure 2, where patient 8 had a gain in chromosomal positions which include 6p21.3, the location of the Msh5 gene. This gain inherently represents an alteration in SEQ ID NO: 1 in a human sample, since at the very least, an extra copy of the gene is present in this patient).

With regard to claim 42, Bentz teaches analysis of tissue samples (see page 1438, column 1, first paragraph).

With regard to claim 44, Bentz teaches analysis using DNA in the sample (see page 1438, column 1, subheading "comparative genomic hybridization").

With regard to claim 45, Bentz teaches that the samples are derived from lymphoma tissue (see page 1438, column 1, first paragraph).

With regard to claim 48, Bentz teaches the use of nick translated digoxigenin labeled DNA, which will inherently comprise two oligonucleotides which will hybridize to SEQ ID NO: 1 (see page 1438, column 1).

Bentz does not connect chromosomal region 6p21 with infertility.

Therman teaches that 6p21 is a chiasmata that is highly preferred (see page 97, column 1). Therman connects these chiasmata to infertility (see page 98, column 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to apply the CGH screening method of Bentz to patients with infertility such as Blooms syndrome since the region of 6p21 has been identified in both patient types as being significant. In particular, CGH is known as a general method to identify differences in the presence of chromosomal regions such as 6p21 and application of CGH to infertile Bloom syndrome patients, who show increased recombination at position 6p21, the position encompassing MSH5, would have been motivated to identify whether this region was significant in the pathology and etiology of Bloom syndrome as taught by Therman.

Response to Arguments

13. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
5/16/07